
Linking the p53 tumour suppressor pathway to somatic cell reprogramming.

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Public Summary:

Reprogramming somatic cells to induced pluripotent stem (iPS) cells has been accomplished by expressing pluripotency factors and oncogenes, but the low frequency and tendency to induce malignant transformation compromise the clinical utility of this powerful approach. We address both issues by investigating the mechanisms limiting reprogramming efficiency in somatic cells. Here we show that reprogramming factors can activate the p53 (also known as Trp53 in mice, TP53 in humans) pathway. Reducing signalling to p53 by expressing a mutated version of one of its negative regulators, by deleting or knocking down p53 or its target gene, p21 (also known as Cdkn1a), or by antagonizing reprogramming-induced apoptosis in mouse fibroblasts increases reprogramming efficiency. Notably, decreasing p53 protein levels enabled fibroblasts to give rise to iPS cells capable of generating germline-transmitting chimaeric mice using only Oct4 (also known as Pou5f1) and Sox2. Furthermore, silencing of p53 significantly increased the reprogramming efficiency of human somatic cells. These results provide insights into reprogramming mechanisms and suggest new routes to more efficient reprogramming while minimizing the use of oncogenes.

Scientific Abstract:

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